

IN THE SPECIFICATION

Please add the following new paragraph on page 2, immediately above the heading titled "Background of the Invention."

-- SEQUENCE LISTING

[003.1] Applicant hereby incorporates herein by reference the "Sequence Listing" filed with the U.S. Patent and Trademark Office on March 30, 2004. The sequence listing was filed in both written (paper) form and in computer readable form comprising one CD-R disc.--

On page 16, please replace paragraph [0068] with the following paragraph:

[0068] Figure 31 illustrates a doublet corresponding to the calculated masses of the d2 ion (glycine-leucine). Figure 32 illustrates the deconvolution of an exemplary mass spectrum. Figure 33 illustrates an overlap of a true 6-residue sequence and a competing 5-residue false sequence. Figure 34 illustrates a general chemical structure exemplifying a core succinic anhydride reactive moiety with a combination of ionizable groups and mass defect elements. Figure 35 illustrates an exemplary synthetic scheme for producing an exemplary succinic anhydride represented in Figure 34. Figure 36 illustrates an exemplary sequencing technique using the Sanger method. Figure 36 also includes the following sequence listings: SEQ ID NO: 5; SEQ ID NO: 6; SEQ ID NO: 7; SEQ ID NO: 8; SEQ ID NO: 9; SEQ ID NO: 10; SEQ ID NO: 11; SEQ ID NO: 12; SEQ ID NO: 13; SEQ ID NO: 14; and SEQ ID NO: 15. Figure 37 A, B, C, and D illustrate modified ddATP, ddGTP, dd TTP, and ddCTP, respectively. Figure 38 illustrates an exemplary deconvolved ddA* and ddG* spectrum. Figure 38 also includes the following sequence listings: SEQ ID NO: 16 and SEQ ID NO: 17. Figure 39 illustrates an exemplary deconvolved ddT* and ddC* spectrum. Figure 39 also includes the following sequence listings: SEQ ID NO: 18; SEQ ID NO: 19; SEQ ID NO: 20; SEQ ID NO: 21; SEQ ID NO: 22; SEQ ID NO: 23; and SEQ ID NO: 24.

On page 50, please replace paragraph [00201] with the following paragraph:

[00201] Further details concerning labeling methods and sequencing methods may be obtained from the following three co-pending applications which are all hereby incorporated herein by reference: (a) U.S. Patent Application Serial No. 09/513,395, filed February 25, 2000 and entitled "Methods for Protein Sequencing;" (b) U.S. Patent Application Serial No. 09/513,907, filed February 25, 2000 and entitled "Polypeptide Fingerprinting and Bioinformatics Database System;" and (c) U.S. Provisional Patent Application Serial No. [[____]] 60/242,165, filed October 19, 2000, by inventors Luke V. Schneider and Michael P. Hall, and entitled "Methods of Sequencing Proteins" (attorney docket no. 020444-000310US).

On page 88, please replace paragraph [00306] with the following paragraph:

[00306] An M13 plasmid carrying a cloned unknown DNA sequence (e.g., d(GTTACAGGAAAT)) (referred to in the Sequence Listing as "SEQ ID NO: 1") is initially hybridized with an M13 origin of replication primer (d(AGTCACGACGACGTTGT)rA) (referred to in the Sequence Listing as "SEQ ID NO: 2") that is labeled at the 3' end with rA to make the primer selectively cleavable by RNase (Integrated DNA Technologies, Inc., Coralville, Iowa). The reaction volume is divided in half and transferred to two tubes. In one tube, polymerase, dNTPs, dGTP, and mass-defect-labeled ddATP* (Figure 37A) and ddGTP* (Figure 37B) are added. To the other tube, polymerase, dNTPs, and mass-defect-labeled ddTTP* (Figure 37C) and ddCTP* (Figure 37D) are added. The modified ddNTPs shown in Figure 37A-D are exemplary and are prepared according to standard procedures (Kricka, L.J., "Nonisotopic DNA Probe Techniques," Academic Press, New York (1992); Keller, G.H. and Manak, M.M., "DNA Probes," Stockton, New York (1989)). As is obvious to those skilled in the art, many other modified ddNTPs are plausible containing purine and pyrimidine bases derivatized with mass defect label moieties and separated by a large assortment of crosslinkers with different lengths and/or compositions. The only requirement is that they are recognized by the DNA polymerase

and can be incorporated into the growing ~~fragment~~ fragment. DNA replication and chain extension is initiated by incubation at 37°C. Mass ladders are produced by chain termination with the ddNTPs. A denaturation and cleavage step with RNase at the end of the reaction removes the chain-terminated product from the template and frees the primer that can be selectively removed by hybridization. The DNA fragments are dissolved in a mass spectrometer-compatible buffer and flown in an ESI-TOF mass spectrometer in negative ion mode. The peaks corresponding to a series of multiply-charged ions for each fragment are deconvolved using standard algorithms supplied by the instrument manufacturer (Applied Biosystems) to generate spectra containing only the zero-charge masses. The zero-charge spectra are subsequently centroided also using the instrument supplier's algorithms.

On page 89, please replace paragraph [00307] with the following paragraph:

[00307] The mass spectral data are analyzed as follows. The spectrum from the ddA*- and ddG*- containing sample is deconvolved and chemical noise is eliminated, leaving only peaks that have incorporated bromine or iodine atoms (Figure 38). The spectrum from the ddT*- and ddC*- containing sample is similarly treated (Figure 39). Looking at both deconvolved spectra, the highest mass fragment is found (4114.733) in the ddA*/ddG* spectrum (Figure 38). It can be further deduced that this fragment contains an iodine mass element as there is no isotopic pair; therefore, the last nucleotide in the "unknown" sequence is A. The mass fragment with the next lower mass is a doublet at 3695.611 and 3697.609 which is found in the ddT*/ddC* spectrum (Figure 39). The doublet indicates incorporation of a bromine atom, and, therefore, the next nucleotide in the sequence is T. This process is repeated until the last peak is found, in this case, a singlet peak at 748.1850 in the ddT*/ddC* spectrum corresponding, therefore, to C. Thus, the sequence ATTCCTGTAAC is determined (referred to in the Sequence Listing as "SEQ ID NO: 3"), and when reversed and the nucleotide complements are substituted, the "unknown" sequence GTTACAGGAAAT is determined (referred to in the Sequence Listing as "SEQ ID NO: 4").

On page 91, please replace paragraph [00311] with the following paragraph:

[00311] This application is also related to co-pending U.S. Patent Application Serial No. **[[_____]] 10/035,349** (Attorney Docket No. **[[.]] 20444-000800US/PCT**), filed on October 19, 2001, by the same three inventors as this application, and entitled "Mass Defect Labelling for Determination of ~~Oligomes~~ Oligomer Sequences", and this co-pending application is hereby incorporated herein by reference in its entirety for all purposes.